Glycosylidene Carbenes

Part 30[1])

Crystal Structure of a Glucose-Derived *N,N*-Unsubstituted Alkoxydiaziridine

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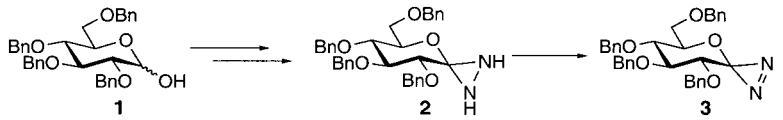
The crystal structure of 1,5-anhydro-2,3,4,6-tetra-*O*-benzyl-1-hydrazi-D-glucitol (**2**) is reported and compared with the structures of other diaziridines. It is the first crystal structure of an *N,N*-unsubstituted diaziridine, noncoordinated at the N-atom, and the first crystal structure of a *C*-alkoxy-diaziridine. Although there is considerable shortening of the C(5)O–C(1) bond, there is no asymmetry in the C(1)–N bond length, the C(5)O, C(1), C(2) plane bisecting the N–N bond. The C(1)–N bonds appear to be slightly shorter and the N–N bond longer than the average for diaziridines, although the structural data for diaziridines do not lend themselves to unequivocal interpretation.

Introduction. – Only eighteen diaziridines have been characterised by their three-dimensional structures, and, except for 3-methyldiaziridine, which was studied by electron diffraction [2], these diaziridines are all either *N*-substituted or coordinated to a metal centre *via* a N-atom. No crystal structure of a *C*-alkoxy diaziridine has been reported so far, even though such structures are of particular interest in the context of the anomeric effect [3].

The glucose-derived diaziridine **2** is the last intermediate in the synthesis of the diazirine **3** [4], a versatile precursor of glycosylidene carbenes [5]. It is prepared from tetra-*O*-benzylglucose **1** in four steps and in an overall yield of 75% [4] (*Scheme*). In $CDCl_3$ solution, **2** is a 95:5 mixture of two 1,2-*trans*-configured diastereoisomers, the major one possessing an intramolecular H-bond to the C(2)–OBn group. The crystal structure of this major diastereoisomer has now been determined.

Scheme



Results and Discussion. – Earlier efforts at growing crystals of **2** suitable for X-ray crystal-structure analysis had failed [4]. Chromatography of **2** with hexane/Et_2O/CH_2Cl_2 (containing 1% of NEt_3) instead of hexane/AcOEt/CH_2Cl_2 has now given samples of **2** that crystallised spontaneously upon removal of the solvent. Long needles

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were obtained by recrystallising **2** in a mixture of NEt_3 and hexane. These crystals were of sufficient quality for an X-ray crystal-structure analysis.

A view of the molecule of **2** is shown in the *Figure*, and selected geometric parameters are listed in *Table 1*. The Bn substituent at C(3) of the glucopyranose ring is disordered in that the atoms of the Ph ring and the CH_2 group occupy two alternative interpenetrating positions which pivot about the *ipso*-C-atom. The major conformation is present in *ca.* 64% of the molecules in the crystal. This disorder has no influence on the conformational or geometric properties of the remaining parts of the molecule.

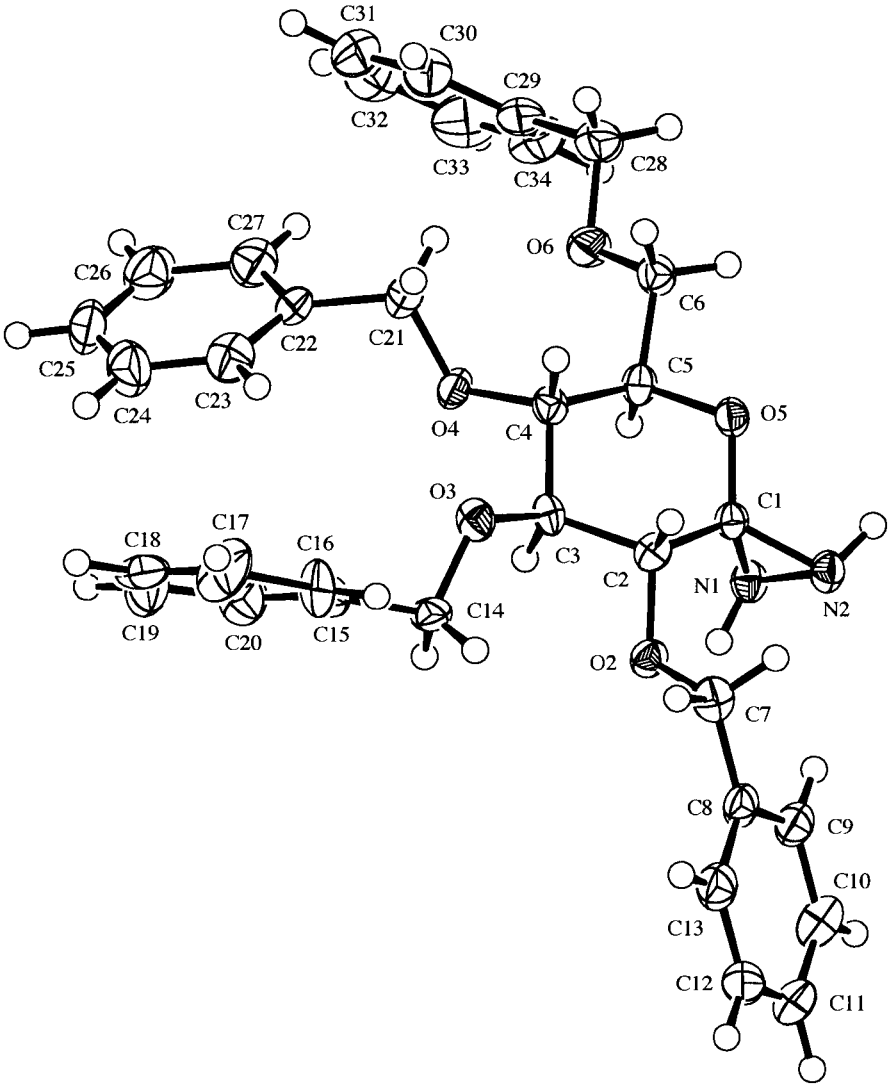

Figure. *A view of the molecular structure of the major conformer of* **2** (50% probability ellipsoids for the non-H-atoms)

Table 1. *Selected Bond Lengths* [Å] *and Bond Angles* [°] *for the Diaziridine* **2**

O(5)–C(1)	1.385(4)	C(1)–C(2)	1.519(4)
O(5)–C(5)	1.451(3)	C(2)–C(3)	1.528(4)
N(1)–C(1)	1.436(4)	C(3)–C(4)	1.524(4)
N(1)–N(2)	1.539(4)	C(4)–C(5)	1.534(4)
N(2)–C(1)	1.426(4)	C(5)–C(6)	1.517(5)
C(1)–N(1)–N(2)	57.17(19)	N(2)–C(1)–C(2)	118.8(2)
C(1)–N(2)–N(1)	57.8(2)	C(1)–C(2)–C(3)	108.5(2)
O(5)–C(1)–C(2)	112.2(2)	C(2)–C(3)–C(4)	113.0(3)
O(5)–C(1)–N(1)	115.5(2)	C(3)–C(4)–C(5)	112.1(2)
O(5)–C(1)–N(2)	117.7(3)	O(5)–C(5)–C(4)	108.0(2)
N(1)–C(1)–N(2)	65.0(2)	C(1)–O(5)–C(5)	111.1(3)
N(1)–C(1)–C(2)	120.2(3)		

The glucopyranose ring has a normal chair conformation, albeit slightly distorted from a perfect chair because of the irregularity in an otherwise perfect cyclohexane structure introduced by the anomeric O-atom. The ring-puckering parameters [6] are $Q = 0.561(3)$ Å, $\theta = 10.5(3)^\circ$ and $\phi = 3(2)^\circ$, and the distortion from an ideal chair conformation is demonstrated by θ, which in an ideal case would have a value of zero.

The hydrazi group possesses the *trans*-configuration, and both N*H* are involved in H-bonding (*Table 2*). The diaziridine ring is oriented such that N(1) is in a pseudo-axial position on the glucopyranose ring, while N(2) is pseudo-equatorial. This means that N(1) is *cis* to the equatorial BnO substituent at C(2) and sufficiently close to O(2) for a N–H···O bonding interaction. Indeed, *H*–N(1) is found on the correct side of the diaziridine ring for such an interaction. It forms a relatively weak intramolecular H-bond with O(2) of the OBn substituent at C(2), thus creating a five-membered loop with a graph set motif of *S*(5) [7]. *H*–N(2) forms an intermolecular H-bond with N(1) of a neighbouring molecule, so that N(1) is both a donor and an acceptor of a H-bond and N(1)–H is part of a cooperative H-bonding system. The intermolecular interaction links the molecules into infinite one-dimensional chains that run parallel to the [001] direction and have a graph set motif of *C*(3). The *trans* configuration of the hydrazi group and the intramolecular H-bond are consistent with the conformation of the major diastereoisomer found in solution, as determined by NMR measurements [4].

Table 2. *Hydrogen-Bonding Geometry for the Diaziridine* **2**

D–H···A[a])	D–H [Å]	H···A [Å]	D···· A [Å]	D–H···A [°]
N(1)–H(1)···O(2)	0.90(3)	2.38(3)	2.840(3)	112(2)
N(2)–H(21)···N(1′)	0.92(4)	2.14(3)	3.015(4)	159(3)

[a]) The primed atom refers to the molecule in the symmetry-related position $\frac{3}{2}-x, 1-y, z-\frac{1}{2}$.

The angle between the planes defined by O(5)–C(1)–C(2) and C(1)–N(1)–N(2) is 88.2(4)°, which indicates no significant distortion of the diaziridine ring from perpendicularity with respect to the lie of the sugar ring. The plane of the diaziridine ring almost bisects the O(5)–C(1)–C(2) angle, as shown by the angles between the diaziridine ring plane, and the C(2)–C(1) and O(5)–C(1) vectors, which are 54.2(3)

and 57.9(3)°, respectively. Furthermore, the diaziridine ring does not pivot about C(1) in an attempt to bring one of the N-atoms closer to an ideal axial or equatorial position; rather the mid-point of the N–N bond almost bisects these positions. The angles between the plane defined by O(5)–C(1)–C(2), and the C(1)–N(1) and C(1)–N(2) vectors are 33.0(4) and 32.0(3)°, respectively. The differences within each of these sets of angles are too small to be significant, and, taken together, these features indicate that the surrounding intramolecular environment has no significant steric or electronic influence on the orientation of the diaziridine ring.

The bond lengths about O(5) (*Table 1*) differ by 0.07 Å, which shows significant asymmetry. Substituted pyranoses usually have more symmetrical C–O bonds about the ring O atom. An almost identical distortion was observed in the structure of 2-acetamido-1,5-anhydro-1-azi-3-*O*-benzyl-4,6-*O*-benzylidene-1,2-dideoxy-D-allitol [8], which contains a diazirine ring spiro-linked to C(1) of a pyranose ring. Thus, both the azi and the hydrazi substituents have similar effects on the electronic nature of the pyranose ring. However, the C(1)–N bonds in **2** differ by only 0.01 Å, and, as this is less than the confidence limits of these distances, the difference is insignificant and suggests that the anomeric effect has very little asymmetric influence on the C(1)–N bonds.

The C–N bonds in the diaziridine ring of **2** are 0.03–0.04 Å shorter than the corresponding bonds in the above-mentioned diazirine and up to 0.06 Å shorter than in other substituted diazirines [8], although 1,1-difluorodiazirine [9] has C–N bonds of lengths similar to those in **2** due to the electronegative effects of the F-atoms. Conversely, the N–N bond of **2** is quite long, and more akin to a C–C bond. For comparison, the sum of the covalent radii of two N-atoms is *ca.* 1.50 Å, and the N–N bond in hydrazine is 1.449(4) Å [10]. In tetrafluorohydrazine, in which the highly electronegative substituents should lead to the weakest N–N bond, this distance is 1.492(7) Å [11]. The only other known three-dimensional structure of an *N*,*N*-unsubstituted organic diaziridine is that of 3-methyldiaziridine, which was studied by electron diffraction [2]. In that structure, the C–N and N–N distances are 1.479(5) and 1.468(7) Å, respectively. Remarkably, the length of the N–N bond in 3-methyldiaziridine is not significantly different from those of the C–N bonds, and all of these bond lengths are in stark contrast to those of **2**.

The *Cambridge Structural Database* [12] lists a further seventeen compounds which contain a diaziridine ring, and for which X-ray crystal-structure determination have been carried out. Of these, twelve are organic compounds with an *N*-substituted diaziridine ring, and five are compounds in which the diaziridine ring is coordinated to a metal centre *via* a N-atom. The diaziridine ring geometry in these compounds varies quite widely. Amongst the organic compounds, the C–N bond lengths vary from 1.33 to 1.51 Å with one outlier at 1.58 Å, while the N–N bond lengths range from 1.45 to 1.61 Å. It is difficult to find a clear correlation between these bond lengths and the substitution pattern of the diaziridine ring. This is partly because of the small sample size of known structures, but also because of the nonsystematic and wide variation in the substitution pattern which does not permit a logical examination of the effect of any particular substituent at any given site on the ring. One clear pattern is that the shortest C–N bonds (1.325 and 1.38(1) Å) and the longest N–N bonds (1.607 and 1.582(9) Å) are observed for the two organic compounds in which the ring C-atom is part of a carbonyl or imino group [13][14]. Conjugation between the lone-pair electrons of the

diaziridine N-atoms and the exocyclic double bond results in significant shortening of the C–N bonds and the corresponding lengthening of the N–N bond. A similar effect is seen in the structure of cyclopropanone [15]. However, aside from these two examples, there does not appear to be any evidence to suggest that longer C–N bonds are necessarily accompanied by a shorter N–N bond. If one excludes these two compounds from the overall comparison, the C–N bond lengths for the organic compounds, including **2** and 3-methyldiaziridine, vary from 1.41 to 1.51 Å (excluding the outlier at 1.58 Å) with an average of 1.45 Å, while the N–N bond lengths range from 1.45 to 1.58 Å with an average of 1.50 Å.

The situation is no clearer for the five compounds in which the diaziridine ring is coordinated to a metal. Here the C–N bond lengths are found to vary from 1.44 to 1.49 Å, while the N–N bond lengths range from 1.38 to 1.52 Å. Part of the difficulty in comparing the geometric parameters of the metal complexes resides in the quite large standard uncertainties of these parameters in some structure determinations, so that C–N or N–N bond lengths, which differ by even as much as 0.1 Å, cannot be distinguished from one another on statistical grounds.

The main conclusion that can be drawn from the structure of **2** regarding the geometry of the diaziridine ring is that the geometry is consistent with that of other diaziridines, but a firm deduction about the influence of the anomeric O-atom of the pyranose ring on the geometry of the diaziridine ring is difficult to make, given the data available. In a discussion on the bonding in diazirines [8], it was concluded that more electronegative substituents at the diazirine C-atom cause shortening of the C–N bond and lengthening of the distal N=N bond. This property has also been observed with cyclopropanes [16], and there is no reason not to expect the same sort of behaviour with diaziridines. The C–N bonds in **2** are among the shortest observed for the known diaziridine structures, and the N–N bond is longer than the average, although not the longest. Unfortunately, the structure of **2** is the only example of a *C*-alkoxy diaziridine, or even of a diaziridine substituted at the ring C-atom by an atom other than a C-atom, excluding the carbonyl and imino examples described above, which, because of the double bond, have other influences on the diaziridine ring bonding. There are no known structures of directly related *C*-halo- or C-hetero-substituted compounds for a comparison of the influence of electronegative substituents. The diaziridine with the most electronegative substituents is a compound that contains two CF_3 substituents at the diaziridine C-atom [17]. Indeed, this compound shows short C–N bonds (1.427 and 1.445 Å), which are quite similar to those in **2**, and an N–N bond length of 1.507 Å. Thus, the pattern of bond lengths within the diaziridine ring of **2** is at least consistent with expectations concerning the influence of electronegative substituents at the ring C-atom. However, a study of more systematically substituted diaziridines would seem to be warranted. A detailed discussion of the orbitals involved in the bonding in diaziridines and the potential effect of substituents, together with some semi-empirical calculations has been presented by *Shustov et al.* [17].

In terms of a possible anomeric effect, the lack of asymmetry in the C(1)–N bonds is consistent with the observation that the plane defined by O(5)–C(1)–C(2) almost bisects the N–N bond. It is not surprising that electron donation from O(5) (evidenced by the asymmetry of the bond lengths about O(5)) to two anomeric substituents, X, symmetrically oriented relative to the donating p(O)-orbital, does not lead to an

asymmetric influence on the anomeric C–X bonds. The lengths of the C(1)–N and the N–N bonds suggest that some of the electron density is transferred to the N–N bond, as best rationalised in a simple, qualitative way by invoking an interaction of the donating O(5) orbital with the antibonding *Walsh* orbital of appropriate orientation and symmetry.

We thank the *Swiss National Science Foundation* and *F. Hoffmann-La Roche AG*, Basel, for generous support.

Experimental Part

General. Solvents for synthesis were freshly distilled; solvents for crystallisation (NEt_3, *puriss.* and hexane, UV-quality) were used as obtained from *Fluka*. TLC: *Merck* silica gel *60F-254* plates; detection by heating with mostain (400 ml of 10% H_2SO_4 soln., 20 g of $(NH_4)_6Mo_7O_{24}\cdot 6H_2O$, 0.4 g of $Ce(SO_4)_2$). Flash chromatography (FC): silica gel *Fluka 60* (0.04–0.063 mm). M.p. uncorrected.

1,5-Anhydro-2,3,4,6-tetra-O-*benzyl-1-hydrazi*-D-*glucitol* (**2**). 2,3,4,6-Tetra-*O*-benzyl-*N*-(methylsulfonyloxy)-D-glucoimido-1,5-lactone (8.3 g, 13.1 mmol) was treated with a sat. soln. of NH_3 in MeOH according to *Briner et al.* [4]. The mixture was stirred at 23° until disappearance (TLC) of the starting material. The solvent was removed *i.v.* at 20°. A suspension of the residue in 50 ml of Et_2O was filtered through a sintered-glass funnel, and the filter cake was washed once with 50 ml of Et_2O. Evaporation of the solvent from the combined filtrates and washings (at 20°) yielded 7.7 g of crude diaziridine as a yellow oil, which was purified by FC on silica (200 g; hexane/Et_2O/CH_2Cl_2 3:1:1 + 1% NEt_3) at 23° to give 4.0 g (55%) of pure **2**. A 300-MHz ^{1}H-NMR ($CDCl_3$) spectrum showed exclusively signals of a 95:5 mixture of two diastereoisomers, in agreement with the data in [4]. R_f (hexane/EtOAc/CH_2Cl_2 3:1:1) 0.25.

Crystallisation of **2**. A sample of **2** (300 mg, 0.54 mmol), prepared as described above, was dissolved in 0.5 ml of NEt_3. Hexane was added at 23°, until the resulting mixture remained slightly turbid. The temp. of the soln. was raised by 1–2°, and the resulting clear soln. was inoculated with **2** and connected *via* a glass tube to a flask containing hexane. Colourless crystals, m.p. 52–53° (NEt_3/hexane), were collected after 1–2 weeks at 23° and subjected to an X-ray crystal-structure analysis.

X-Ray Crystal-Structure Determination of **2** (see *Table 3* and *Fig.*)[2]). All measurements were conducted at low-temp. on a *Rigaku AFC5R* diffractometer using graphite-monochromated MoK_α radiation ($\lambda = 0.71069$ Å) and a 12-kW rotating-anode generator. The ω scan mode was employed for data collection. The intensities were corrected for *Lorentz* and polarisation effects, and an empirical absorption correction, based on azimuthal scans of several reflections [18], was also applied. Data collection and refinement parameters are given in *Table 3*, and a view of the molecule is shown in the *Figure*.

The structure was solved by direct methods using SIR92 [19]. The BnO substituent at C(3) is disordered in that the Ph ring and the CH_2 group occupy two alternative positions which pivot about the *ipso*-C-atom. Two positions were defined for the CH_2(14) group, and the five free Ph C-atoms. The site-occupation factors of each orientation were refined, while constraining the total occupancy to 1.0. This yielded an occupancy of 0.64(2) for the major conformation. The bond lengths involving C(14), C(14a), and all Ph ring atoms of the disordered ring were restrained to appropriate distances, and a pseudo-isotropic restraint was also applied to the atomic displacement parameters of three Ph-ring atoms (C(17), C(18), C(19)) in the minor conformation.

All of the non-H atoms were refined anisotropically. All of the H-atoms bonded to C were placed in geometrically calculated positions and refined using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{eq}$ of its parent C-atom. The diaziridine H-atoms were located in a difference-electron-density map, and their positions were allowed to refine together with individual isotropic displacement parameters. Refinement of the structure [20] was carried out on F^2 by full-matrix least-squares procedures, which minimised the function $\Sigma w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was not applied. The absolute configuration of the molecule has not been determined. The

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[2]) The crystallographic data (excluding structure factors) have been deposited with the *Cambridge Crystallographic Data Centre* as supplementary publication no. CCDC-171804. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ (fax: +44-(0)1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

Table 3. *Crystallographic Data for the Diaziridine* **2**

Crystallised from	NEt_3/hexane
Empirical formula	$C_{34}H_{36}N_2O_5$
Formula weight [g mol^{-1}]	552.67
Crystal colour, habit	colourless, needle
Crystal dimensions [mm]	$0.19 \times 0.20 \times 0.50$
Temp. [K]	173(1)
Crystal system	orthorhombic
Space group	$P2_12_12_1$ (#19)
Z	4
Reflections for cell determination	24
2θ Range for cell determination [°]	20 – 36
Unit-cell parameters a [Å]	21.780(4)
b [Å]	27.821(4)
c [Å]	4.753(4)
V [Å^3]	2880(3)
D_x [g cm^{-3}]	1.275
μ(MoK_α) [mm^{-1}]	0.0853
Transmission factors (min; max)	0.915; 1.000
$2\theta_{(max)}$ [°]	55
Total reflections measured	4864
Symmetry-independent reflections	4682
Observed reflections [$I > 2\sigma(I)$]	3008
Reflections used in refinement	4682
Parameters refined	433
Restraints	34
Final $R(F)$ [$I > 2\sigma(I)$ reflections]	0.0510
$wR(F^2)$ (all data)	0.1449
Weights	$w = 1/[\sigma^2(F_o^2) + (0.067P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
Goodness-of-fit on F^2	1.015
Final Δ_{max}/σ	0.001
$\Delta\rho$ (max; min) [e Å^{-3}]	0.22; -0.25

enantiomer used in the structural model for the refinement was chosen to agree with the known D-*gluco* configuration. Neutral-atom-scattering factors for non-H-atoms were taken from [21], and the scattering factors for H-atoms were taken from [22]. Anomalous dispersion effects were included in F_c [23]; the values for f' and f'' were those of [24]. The values of the mass attenuation coefficients were taken from [25]. Calculations were performed using SHELXL97 [20] and the teXsan crystallographic software package [26], and the crystallographic diagram was drawn using ORTEPII [27].

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Received October 17, 2001